FIGURE 1.

GCGCGCCGGC CTGAGAGCCC TGTGGACAAC CTCGTCATTG TCAGGCACAG
AGCGGTAGAC CCTGCTTCTC TAAGTGGGCA GCGGACAGCG GCACGCACAT
TTCACCTGTC CCGCAGACAA CAGCACCATC TGCTTGGGAG AACCCTCTCC
CTTCTCTGAG AAAGAAAGAT GTCGAATGGG TATTCCACAG ACGAGAATTT
CCGCTATCTC ATCTCGTGCT TCAGGGCCAG GGTGAAAATG TACATCCAGG
TGGAGCCTGT GCTGGACTAC CTGACCTTTC TGCCTGCAGA GGTGAAGGAG
CAGATTCAGA GGACAGTCGC CACCTCCGGG AACATGCAGG CAGTTGAACT
GCTGCTGAGC ACCTTGGAGA AGGGAGTCTG GCACCTTGGT TGGACTCGGG
AATTCGTGGA GGCCCTCCGG AGAACCGGCA GCCCTCTGGC CGCCCGCTAC
ATGAACCCTG AGCTCACGGA CTTGCCCTCT CCATCGTTTG AGAACGCTCA
TGATGAATAT CTCCAACTGC TGAACCTCCT TCAGCCCACT CTGGTGGACA
AGCTTCTAGT TAGAGACGTC TTGGATAAGT GCATGGAGGA GGAACTGTTG
ACAATTGAAG ACAGAAACCG GATTGCTGCT GCAGAAAACA ATGGAAATGA
ATCAGGTGTA AGAGAGCTAC TAAAAAGGAT TGTGCAGAAA GAAAACTGGT
TCTCTGCATT TCTGAATGTT CTTCGTCAAA CAGGAAACAA TGAACTTGTC
CAAGAGTTAA CAGGCTCTGA TTGCTCAGAA AGCAATGCAG AGATTGAGAA
TTTATCACAA GTTGATGGTC CTCAAGTGGA AGAGCAACTT CTTTCAACCA
CAGTTCAGCC AAATCTGGAG AAGGAGGTCT GGGGCATGGA GAATAACTCA
TCAGAATCAT CTTTTGCAGA TTCTTCTGTA GTTTCAGAAT CAGACACAAG
TTTGGCAGAA GGAAGTGTCA GCTGCTTAGA TGAAAGTCTT GGACATAACA
GCAACATGGG CAGTGATTCA GGCACCATGG GAAGTGATTC AGATGAAGAG
AATGTGGCAG CAAGAGCATC CCCGGAGCCA GAACTCCAGC TCAGGCCTTA
CCAAATGGAA GTTGCCCAGC CAGCCTTGGA AGGGAAGAAT ATCATCATCT
GCCTCCCTAC AGGGAGTGGA AAAACCAGAG TGGCTGTTTA CATTGCCAAG
GATCACTTAG ACAAGAAGAA AAAAGCATCT GAGCCTGGAA AAGTTATAGT
TCTTGTCAAT AAGGTACTGC TAGTTGAACA GCTCTTCCGC AAGGAGTTCC
AACCATTTTT GAAGAAATGG TATCGTGTTA TTGGATTAAG TGGTGATACC
CAACTGAAAA TATCATTTCC AGAAGTTGTC AAGTCCTGTG ATATTATTAT
CAGTACAGCT CAAATCCTTG AAAACTCCCT CTTAAACTTG GAAAATGGAG
AAGATGCTGG TGTTCAATTG TCAGACTTTT CCCTCATTAT CATTGATGAA
TGTCATCACA CCAACAAAGA AGCAGTGTAT AATAACATCA TGAGGCATTA
TTTGATGCAG AAGTTGAAAA ACAATAGACT CAAGAAAGAA AACAAACCAG
TGATTCCCCT TCCTCAGATA CTGGGACTAA CAGCTTCACC TGGTGTTGGA
GGGGCCACGA AGCAAGCCAA AGCTGAAGAA CACATTTTAA AACTATGTGC

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CAATCTTGAT GCATTTACTA TTAAAACTGT TAAAGAAAAC CTTGATCAAC
TGAAAAACCA AATACAGGAG CCATGCAAGA AGTTTGCCAT TGCAGATGCA
ACCAGAGAAG ATCCATTTAA AGAGAAACTT CTAGAAATAA TGACAAGGAT
TCAAACTTAT TGTCAAATGA GTCCAATGTC AGATTTTGGA ACTCAACCCT
ATGAACAATG GGCCATTCAA ATGGAAAAAA AAGCTGCAAA AAAAGGAAAT
CGCAAAGAAC GTGTTTGTGC AGAACATTTG AGGAAGTACA ATGAGGCCCT
ACAAATTAAT GACACAATTC GAATGATAGA TGCGTATACT CATCTTGAAA
CTTTCTATAA TGAAGAGAAA GATAAGAAGT TTGCAGTCAT AGAAGATGAT
AGTGATGAGG GTGGTGATGA TGAGTATTGT GATGGTGATG AAGATGAGGA
TGATTTAAAG AAACCTTTGA AACTGGATGA AACAGATAGA TTTCTCATGA
CTTTATTTTT TGAAAACAAT AAAATGTTGA AAAGGCTGGC TGAAAACCCA
GAATATGAAA ATGAAAAGCT GACCAAATTA AGAAATACCA TAATGGAGCA
ATATACTAGG ACTGAGGAAT CAGCACGAGG AATAATCTTT ACAAAAACAC
GACAGAGTGC ATATGCGCTT TCCCAGTGGA TTACTGAAAA TGAAAAATTT
GCTGAAGTAG GAGTCAAAGC CCACCATCTG ATTGGAGCTG GACACAGCAG
TGAGTTCAAA CCCATGACAC AGAATGAACA AAAAGAAGTC ATTAGTAAAT
TTCGCACTGG AAAAATCAAT CTGCTTATCG CTACCACAGT GGCAGAAGAA
GGTCTGGATA TTAAAGAATG TAACATTGTT ATCCGTTATG GTCTCGTCAC
CAATGAAATA GCCATGGTCC AGGCCCGTGG TCGAGCCAGA GCTGATGAGA
GCACCTACGT CCTGGTTGCT CACAGTGGTT CAGGAGTTAT CGAACATGAG
ACAGTTAATG ATTTCCGAGA GAAGATGATG TATAAAGCTA TACATTGTGT
TCAAAATATG AAACCAGAGG AGTATGCTCA TAAGATTTTG GAATTACAGA
TGCAAAGTAT AATGGAAAAG AAAATGAAAA CCAAGAGAAA TATTGCCAAG
CATTACAAGA ATAACCCATC ACTAATAACT TTCCTTTGCA AAAACTGCAG
TGTGCTAGCC TGTTCTGGGG AAGATATCCA TGTAATTGAG AAAATGCATC
ACGTCAATAT GACCCCAGAA TTCAAGGAAC TTTACATTGT AAGAGAAAAC
AAAGCACTGC AAAAGAAGTG TGCCGACTAT CAAATAAATG GTGAAATCAT
CTGCAAATGT GGCCAGGCTT GGGGAACAAT GATGGTGCAC AAAGGCTTAG
ATTTGCCTTG TCTCAAAATA AGGAATTTTG TAGTGGTTTT CAAAAATAAT
TCAACAAAGA AACAATACAA AAAGTGGGTA GAATTACCTA TCACATTTCC
CAATCTTGAC TATTCAGAAT GCTGTTTATT TAGTGATGAG GATTAGCACT
TGATTGAAGA TTCTTTTAAA ATACTATCAG TTAAACATTT AATATGATTA
TGATTAATGT ATTCATTATG CTACAGAACT GACATAAGAA TCAATAAAAT
GATTGTTTTA CTCTG

FIGURE 2.

MSNGYSTDEN FRYLISCFRA RVKMYIQVEP VLDYLTFLPA EVKEQIQRTV
ATSGNMQAVE LLLSTLEKGV WHLGWTREFV EALRRTGSPL AARYMNPELT
DLPSPSFENA HDEYLQLLNL LQPTLVDKLL VRDVLDKCME EELLTIEDRN
RIAAAENNGN ESGVRELLKR IVQKENWFSA FLNVLRQTGN NELVQELTGS
DCSESNAEIE NLSQVDGPQV EEQLLSTTVQ PNLEKEVWGM ENNSSESSFA
DSSVVSESDT SLAEGSVSCL DESLGHNSNM GSDSGTMGSD SDEENVAARA
SPEPELQLRP YQMEVAQPAL EGKNIIICLP TGSGKTRVAV YIAKDHLDKK
KKASEPGKVI VLVNKVLLVE QLFRKEFQPF LKKWYRVIGL SGDTQLKISF
PEVVKSCDII ISTAQILENS LLNLENGEDA GVQLSDFSLI IIDECHHTNK
EAVYNNIMRH YLMQKLKNNR LKKENKPVIP LPQILGLTAS PGVGGATKQA
KAEEHILKLC ANLDAFTIKT VKENLDQLKN QIQEPCKKFA IADATREDPF
KEKLLEIMTR IQTYCQMSPM SDFGTQPYEQ WAIQMEKKAA KKGNRKERVC
AEHLRKYNEA LQINDTIRMI DAYTHLETFY NEEKDKKFAV IEDDSDEGGD
DEYCDGDEDE DDLKKPLKLD ETDRFLMTLF FENNKMLKRL AENPEYENEK
LTKLRNTIME QYTRTEESAR GIIFTKTRQS AYALSQWITE NEKFAEVGVK
AHHLIGAGHS SEFKPMTQNE QKEVISKFRT GKINLLIATT VAEEGLDIKE
CNIVIRYGLV TNEIAMVQAR GRARADESTY VLVAHSGSGV IEHETVNDFR
EKMMYKAIHC VQNMKPEEYA HKILELQMQS IMEKKMKTKR NIAKHYKNNP
SLITFLCKNC SVLACSGEDI HVIEKMHHVN MTPEFKELYI VRENKALQKK
CADYQINGEI ICKCGQAWGT MMVHKGLDLP CLKIRNFVVV FKNNSTKKQY
KKWVELPITF PNLDYSECCL FSDED•

FIGURE 3

gcacattttg	cctacaaag	accttattg	taaggcaga	cctgctggg
aaaacaaaat	tccgccgga	gagctttgt	gagcgttgg	cttggtgtc
agagagaatt	gctttcctt	tctgtttcc	gcggtgtcc	taaccaaag
gcctcctctc	tcacccgcc	cgaccaaaa	gtggcgtct	cctgaggaa
actccctccc	gccaggcag	ttacgttta	aaagtcctg	gaagagaat
cgaaacagaa	ccaaagtca	gcaaactct	taagaactg	ctgacagaa
agctggactc	aagctccta	ccgagtgtg	agcaggatc	ccccggtcc
gggaccccag	cgcacaccg	agagtccaa	gtgccgcgc	tgccggccg
cacctgcctg	cgcggcccc	cgcgccgcc	cgctgccca	ctgcccgcc
tgcccacctg	ccaggtgcg	gtgcagccc	gcgcgccgg	ctgagagcc
ctgtggacaa	ctcgtcatt	tcaggcaca	agcggtaga	cctgcttct
ntaagtgggc	gcggacagc	gcacgcaca	ttcacctgt	ccgcagaca
ctgcttggga	aaccctctc	cttctctga	aaagaaaga	gtcgaatgg
gtattccaca	acgagaatt	ccgctatct	atctcgtgc	tcagggcca
gggtgaaaat	tacatccag	tggagcctg	gctggacta	ctgaccttt
ctgcctgcag	ggtgaagga	cagattcag	ggacagtcg	cacctccgg
gaacatgcag	cagttgaac	gctgctgag	accttggag	agggagtct
ggcaccttgg	tggactcgg	aattcgtgg	ggccctccg	agaaccggc
agccctctgg	cgcccgcta	atgaaccct	agctcacgg	cttgccctc
tccatcgttt	agaacgctc	tgatgaata	ctccaactg	tgaacctcc
ttcagcccac	ctggtggac	agctt		

FIGURE 4

```
MDA-5    SPEPELQLRPYQMEVAQPALEGKNIIICLPTGSGKTRVAVYIAKDH-LDKKKKA---SEP 356
Q9HAM6   -----MELRSYQWEVIMPALEGKNIIIWLPTGAGKTRAAAYVAKRH-LET-------VDG 47
RHIV-1   HTYSPLKPRKYQLELALPAQNGKNTIICAPTGCGKTFVSLLICEHH-LKKFPR----GRK 288
RIG-1    NLYSPFKPRNYQLELALPAMKGKNTIICAPTGCGKTFVSLLICEHH-LKKFPQ----GQK 290
P34529   ADLQCFNPRDYQVELLDKATK-KNTIVQLGTGSGKTFIAVLLLKEYGVQLFAPL---DQG 61
Q9SP32   EKVVEEQARRYQLDVLEQAKA-KNTIAFLETGAGKTLIAILLIKSVHKDLMSQ-----NR 295
Q09884   SFLLPQLLRKYQQDVYNIASK-QNTLLVMRTGAGKTLLAVKLIKQKLEEQILIQESNLEH 63
               * **  ::    *     :* :    **.***    :    : :     .
                       i                 TGxGKTxxxL(I)

MDA-5    GK-VIVLVNKVLLVEQLFR--KEFQPFLKKWYRVIGLSGDTQLKISFPEVVKSCDIIIST 413
Q9HAM6   AK-VVVLVNRVHLVTQHG---EEFRRMLDGRWTVTTLSGDMGPRAGFGHLARCHDLLICT 103
RHIV-1   GK-VVFFAIQLPVYEQQKS--VFSKHFERLGYKVAGISGATSDTVCVEQIVENSDIIILT 345
RIG-1    GK-VVFFANQIPVYEQQKS--VFSKYFERHGYRVTGISGATAENVPVEQIVENNDIIILT 347
P34529   GKRAFFVVEKVNLVEQQAIHIEVHTSFKVGQVHGQTSSGLWDSKEQCDQFMKRHHVVVIT 121
Q9SP32   KMLSVFLVPKVPLVYQQAEVIRNQTCFQVGHYCGEMGQDFWDSR-RWQREFESKQVLVMT 354
Q09884   KKISVFLVNKVPLVFQQAEYIRSQLPAKVGMFYGELS--IEMSEQLLTNIILKYNVIVIT 121
             .... :: :   *                               .       .::: *
                         ii                                          T(Ic)

MDA-5    AQILENSLLNLENGEDAGVQLSDFSLIIIDECHHTN-KEAVYNNIMRHYLMQKLKNNRLK 472
Q9HAM6   AELLQMALTSPE--EEEHVELTVFSLIVVDECHHTH-KDTVYNVIMSQYLELKLQR---- 156
RHIV-1   PQILVNCLTNGT-----IPSLSVFTLMIFDECHNTS-KQHPYNVIMFSYLDRKLGGS--- 396
RIG-1    PQILVNNLKKGT-----IPSLSIFTLMIFDECHNTS-KQHPYNMIMFNYLDQKLGGS--- 398
P34529   AQCLLDLIRHAY------LKIEDMCVLIFDECHHALGSQHPYRSIMVDYKLLKKDK---- 171
Q9SP32   AQILLNILRHSI------IRMETIDLLILDECHHAV-KKHPYSLVMSEFYHTTPKDK--- 404
Q09884   ADLFYLFLARGF------LSINDLNLIIFDECHHAI-GNDAYARIMNDFYHRAKAVLS-- 172
         .: :    :                 :    : :::.****::   .   *   :*   :
                                        DECH(II)          iii

MDA-5    KENKPVIPLPQILGLTASPG-VGGATKQAKAEEHILKLCANLDAFTIKTVKENLDQLKNQ 531
Q9HAM6   ------AQPLPQVLGLTASPG-TGGASKLDGAINHVLQLCANLDTWCIMSPQNCCPQLQEH 210
RHIV-1   -----SDSLPQVIGLTASVG-VGDAKNKAEATEYICKLCASLDTSVIATVRDNLEELEEV 450
RIG-1    -----SGPLPQVIGLTASVG-VGDAKNTDEALDYICKLCASLDASVIATVKHNLEELEQV 452
P34529   -------PVPRVLGLTASL--IKAKVAPEKLMEQLKKLESAMDS--VIETASDLVSLSKY 220
Q9SP32   --------RPAIFGMTASPVNLKGVSSQVDCAIKIRNLETKLDS--TVCTIKDRKELEKH 454
Q09884   ---KKHFTLPRIFGMTASPF----TGKKGNLYHRLYQWEQLFDSKAHVVSEN---ELADY 222
               *  ::*:***                 :  :      :*:            .*  .
                 SAT(III)                           iv            v

MDA-5    IQEPCKKFAIADATREDP-FKEKLLEIMTRIQTYCQ-----------------MSPMS- 571
Q9HAM6   SQQPCKQYNLCHRRSQDP-FGDLLKKLMDQIHDHLE-----------------MPELSR 251
RHIV-1   VYKPQKFFRKVELRTTDR-FKCIISQLMMEIESLAKSIFEELGTITL----GGLFQIQNS 505
RIG-1    VYKPQKFFRKVESRISDK-FKYIIAQLMRDTESLAKRICKDLENLS----------QIQNR 502
P34529   GAKPYEVVIICKDFEIGC-LGIPNFDTVIEIFDETVAFVN-------------TTTEFHP 266
Q9SP32   VPMPSEIVVEYDKAATMWSLHETIKQMIAAVEEAAQASSRKSKWQFMGARDAGAKDELRQ 514
Q09884   FCLPEESYVMYSNKLVVP----PSDSIIKKCEETLQG------------------CKLISR 261
            * :                .  :
            vi

MDA-5    ENNKMLKRLAENPEYENEKLTKLRNTIMEQYTR------TEESARGIIFTKTRQSAYALS 735
Q9HAM6   DRKNELAHLATHG-PENPKLEMLEKILQRQFS-------SSNSPRGIIFTRTRQSAHSLL 384
RHIV-1   EKLQELESISIDPSNENPKLRDLCFILQEEYHL------NPET-RTILFVKTRALVDALK 647
RIG-1    EKLQELESVSRDPSNENPKLEDLCFILQEEYHL------NPET-ITILFVKTRALVDALK 644
P34529   KKIKSIEALRPYVPQRVIRLFEILETFNPEFQKERMKLEKAEHLSAIIFVDQRYIAYSLL 401
Q9SP32   EHVDEVIGAAVADGKVTPKVQSLIKLLLKYQHT--------ADFRAIVFVERVVAALVLP 681
Q09884   YSDNGPRIPVFDSTDVTDKVFKLLELLKATYRK-------SDSVRTVIFVERKATAFTLS 378
             .                 :: :  :                     ::*.    .  *
                                                          FXXS(IV)   vii

MDA-5    QWITENEKFAE--VGVKAHHLIGAGHSSEFKPMTQ---NEQKEVISKFRTG-KINLLIAT 789
Q9HAM6   LWLQQQQGLQT--VDIRAQLLIGAGNSSQSTHMTQ---RDQQEVIQKFQDG-TLNLLVAT 438
RHIV-1   KWIKENPKLS----FLKPSILTGRGKTNQNIGMTL---PAQKCVLDTFRTDKDNKILITT 700
RIG-1    NWIEGNPKLS----FLKPGILTGRGKTNQNTGMTL---PAQKCILDAFKASGDHNILIAT 697
P34529   LMMRHIKSWEPKFKFVNPDYVVGASGRNLASSDSQGLHKRQTEVLRRFHRN-EINCLIAT 460
Q9SP32   KVFAELPSLS----FIRCASMIGHNNSQEMKSSQM------QDTISKFRDG-HVTLLVAT 730
Q09884   LFMKTLNLPN-----IRAHSFIGHGPSDQGEFSMT--FRRQKDTLHKFKTG-KYNVLIAT 430
         :             :.   . * .  .                  :  *:  .   .*::*
                               viii                       ix       T(V)

MDA-5    TVAEEGLDIKECNIVIRYGLVTNEIAMVQARGRARADESTYVLVAHSG------------ 837
Q9HAM6   SVAEEGLDIPHCNVVVRYGLLTNEISMVQARGRAWADQSVYAFVATEG------------ 486
RHIV-1   SVADEGIDIAQCNLVILYEYVGNVIKMIQTRGRGRARGSKCFLLTAN------------- 747
RIG-1    SVADEGIDIAQCNLVILYEYVGNVIKMIQTRGRGRARGSKCFLLTSN------------- 744
P34529   SVLEEGVDVKQCNLVIKFDRPLDMRSYVQSKGRARRAGSRYVITVEEK------------ 508
Q9SP32   SVAEEGLDIRQCNVVMRFDLAKTVLAYIQSRGRARKPGSDYILMVERGNVSHAAFLRNAR 790
Q09884   AVAEEGIDVPSCNLVIRFNICRTVTQYVQSRGRARAMASKFLIFLNTEELLIHERILHE- 489
         :* :**:*: **.*:*:            :*::**.    *  :
         VID(Va)        x              QRxGRxGR(VI)
```

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FIGURE 5 A-D

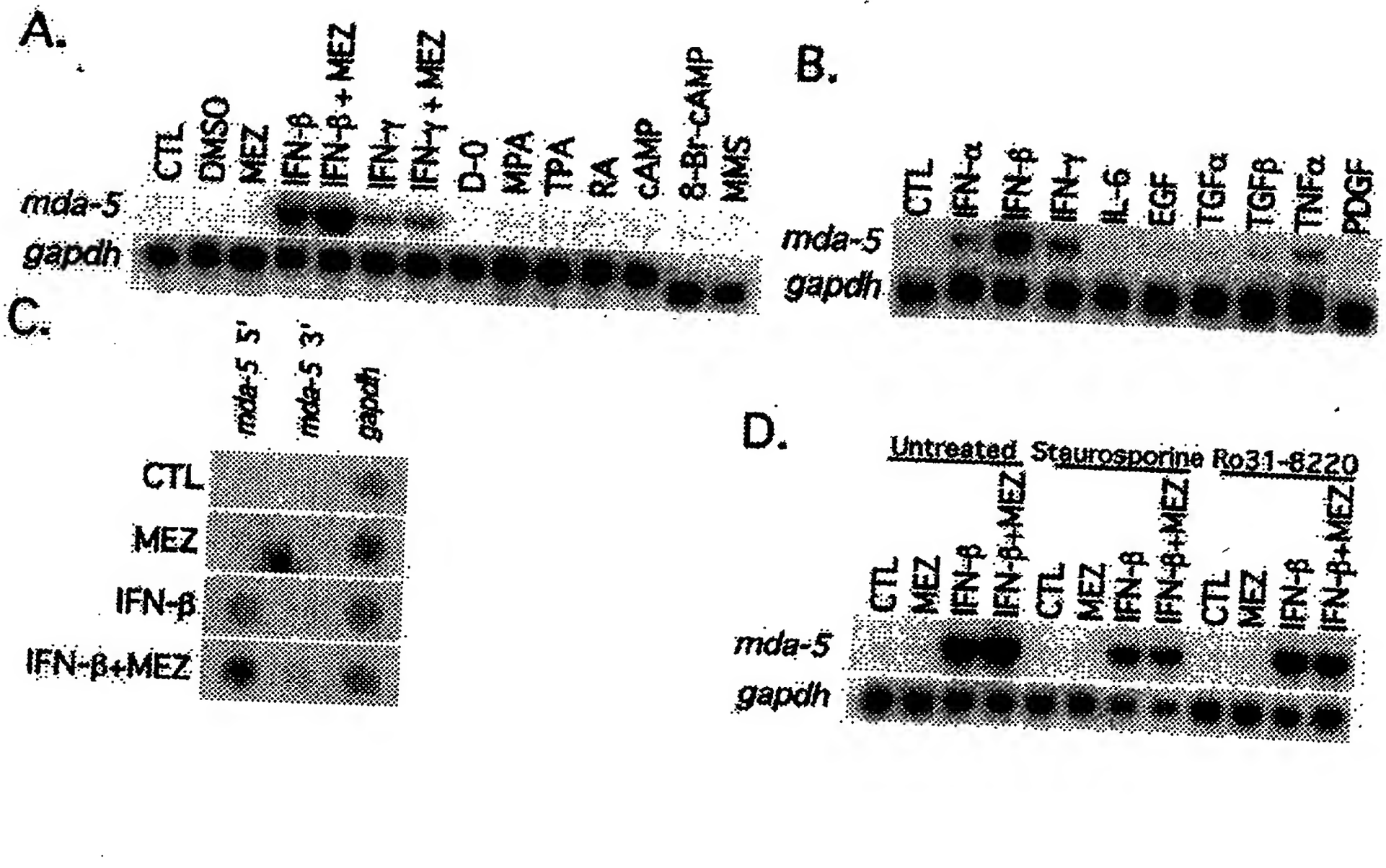
A.
CTL
DMSO
MEZ
IFN-β
IFN-β + MEZ
IFN-γ
IFN-γ + MEZ
D-0
MPA
TPA
RA
cAMP
8-Br-cAMP
MMS
mda-5
gapdh
B.
CTL
IFN-α
IFN-β
IFN-γ
IL-6
EGF
TGFα
TGFβ
TNFα
PDGF
mda-5
gapdh
C.
mda-5 5'
mda-5 3'
gapdh
CTL
MEZ
IFN-β
IFN-β+MEZ
D.
Untreated
Staurosporine
Ro31-8220
CTL
MEZ
IFN-β
IFN-β+MEZ
mda-5
gapdh

FIGURE 6 A-B

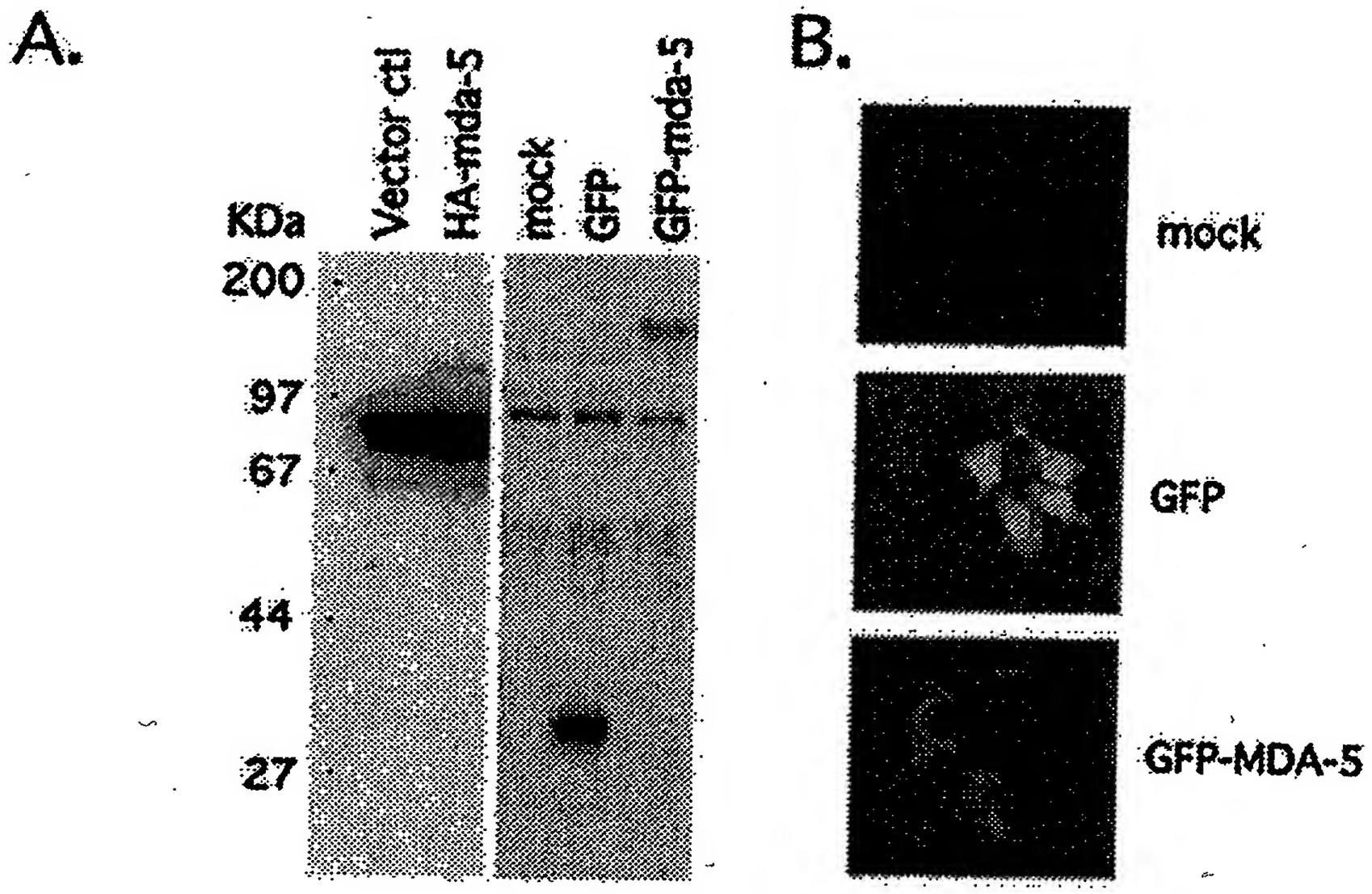
A.
Vector ctl
HA-mda-5
mock
GFP
GFP-mda-5
KDa
200
97
67
44
27
B.
mock
GFP
GFP-MDA-5

FIGURE 7 A-B

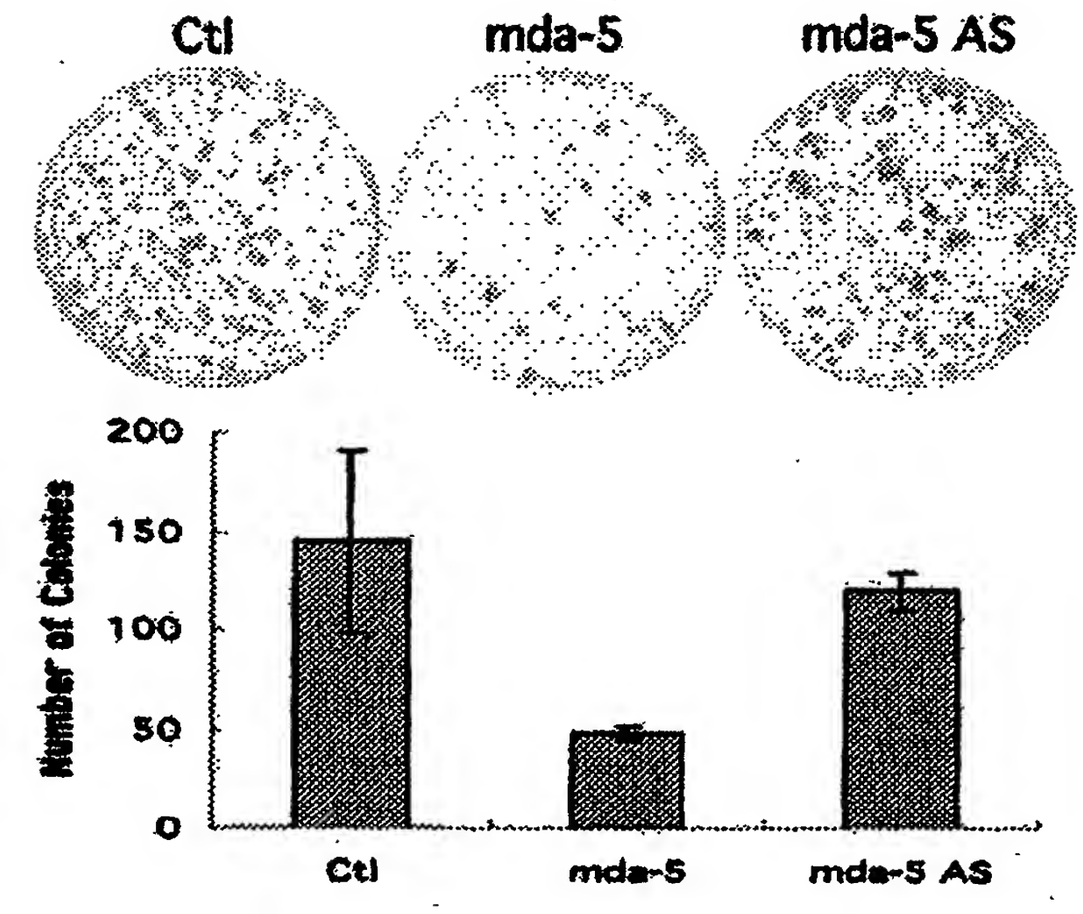
A.
Ctl
mda-5
mda-5 AS
B.
Number of Colonies
200
150
100
50
0
Ctl
mda-5
mda-5 AS

FIGURE 8 A-D

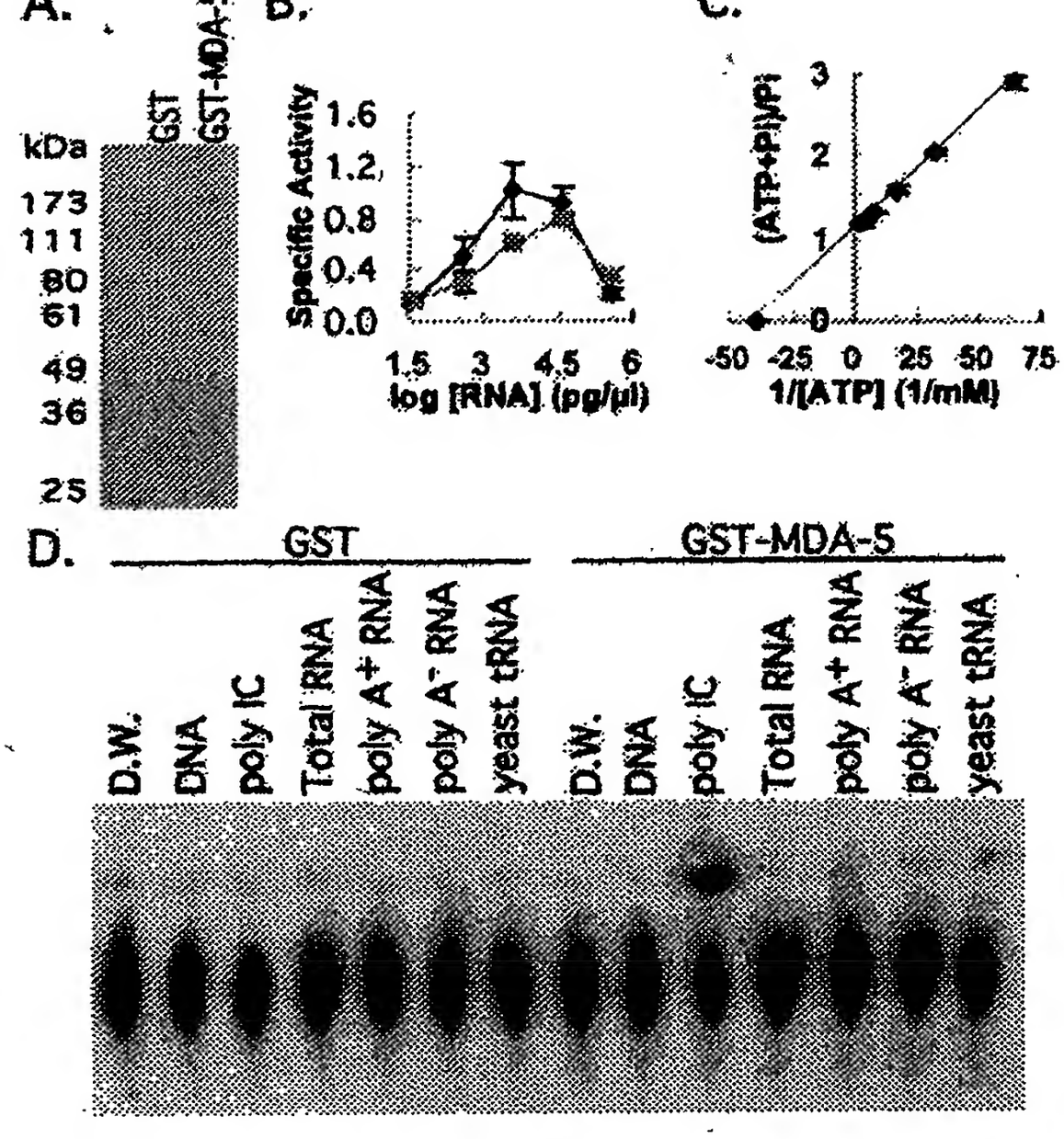
A.
B.
C.
GST
GST-MDA-5
kDa
173
111
80
61
49
36
25
Specific Activity
1.6
1.2
0.8
0.4
0.0
1.5
3
4.5
6
log [RNA] (pg/µl)
(ATP+Pi)/Pi
3
2
1
0
-50
-25
0
25
50
75
1/[ATP] (1/mM)
D.
GST
GST-MDA-5
D.W.
DNA
poly IC
Total RNA
poly A+ RNA
poly A- RNA
yeast tRNA

FIGURE 9

GCGCGCCGGC CTGAGAGCCC TGTGGACAAC CTCGTCATTG TCAGGCACAG
AGCGGTAGAC CCTGCTTCTC TAAGTGGGCA GCGGACAGCG GCACGCACAT
TTCACCTGTC CCGCAGACAA CAGCACCATC TGCTTGGGAG AACCCTCTCC
CTTCTCTGAG AAAGAAAGAT GTCGAATGGG TATTCCACAG ACGAGAATTT
CCGCTATCTC ATCTCGTGCT TCAGGGCCAG GGTGAAAATG TACATCCAGG
TGGAGCCTGT GCTGGACTAC CTGACCTTTC TGCCTGCAGA GGTGAAGGAG
CAGATTCAGA GGACAGTCGC CACCTCCGGG AACATGCAGG CAGTTGAACT
GCTGCTGAGC ACCTTGGAGA AGGGAGTCTG GCACCTTGGT TGGACTCGGG
AATTCGTGGA GGCCCTCCGG AGAACCGGCA GCCCTCTGGC CGCCCGCTAC
ATGAACCCTG AGCTCACGGA CTTGCCCTCT CCATCGTTTG AGAACGCTCA
TGATGAATAT CTCCAACTGC TGAACCTCCT TCAGCCCACT CTGGTGGACA
AGCTTCTAGT TAGAGACGTC TTGGATAAGT GCATGGAGGA GGAACTGTTG
ACAATTGAAG ACAGAAACCG GATTGCTGCT GCAGAAAACA ATGGAAATGA
ATCAGGTGTA AGAGAGCTAC TAAAAAGGAT TGTGCAGAAA GAAAACTGGT
TCTCTGCATT TCTGAATGTT CTTCGTCAAA CAGGAAACAA TGAACTTGTC
CAAGAGTTAA CAGGCTCTGA TTGCTCAGAA AGCAATGCAG AGATTGAGAA
TTTATCACAA GTTGATGGTC CTCAAGTGGA AGAGCAACTT CTTTCAACCA
CAGTTCAGCC AAATCTGGAG AAGGAGGTCT GGGGCATGGA GAATAACTCA
TCAGAATCAT CTTTTGCAGA TTCTTCTGTA GTTTCAGAAT CAGACACAAG
TTTGGCAGAA GGAAGTGTCA GCTGCTTAGA TGAAAGTCTT GGACATAACA
GCAACATGGG CAGTGATTCA GGCACCATGG GAAGTGATTC AGATGAAGAG
AATGTGGCAG CAAGAGCATC TCCGGAGCCA GAACTCCAGC TCAGGCCTTA
CCAAATGGAA GTTGCCCAGC CAGCCTTGGA AGGGAAGAAT ATCATCATCT
GCCTCCCTAC AGGGAGTGGA AAAACCAGAG TGGCTGTTTA CATTGCCAAG
GATCACTTAG ACAAGAAGAA AAAAGCATCT GAGCCTGGAA AAGTTATAGT
TCTTGTCAAT AAGGTACTGC TAGTTGAACA GCTCTTCCGC AAGGAGTTCC
AACCATTTTT GAAGAAATGG TATCGTGTTA TTGGATTAAG TGGTGATACC
CAACTGAAAA TATCATTTCC AGAAGTTGTC AAGTCCTGTG ATATTATTAT
CAGTACAGCT CAAATCCTTG AAAACTCCCT CTTAAACTTG GAAAATGGAG
AAGATGCTGG TGTTCAATTG TCAGACTTTT CCCTCATTAT CATTGATGAA
TGTCATCACA CCAACAAAGA AGCAGTGTAT AATAACATCA TGAGGCATTA
TTTGATGCAG AAGTTGAAAA ACAATAGACT CAAGAAAGAA AACAAACCAG
TGATTCCCCT TCCTCAGATA CTGGGACTAA CAGCTTCACC TGGTGTTGGA
GGGGCCACGA AGCAAGCCAA AGCTGAAGAA CACATTTTAA AACTATGTGC
CAATCTTGAT GCATTTACTA TTAAAACTGT TAAAGAAAAC CTTGATCAAC
TGAAAAACCA AATACAGGAG CCATGCAAGA AGTTTGCCAT TGCAGATGCA
ACCAGAGAAG ATCCATTTAA AGAGAAACTT CTAGAAATAA TGACAAGGAT
TCAAACTTAT TGTCAAATGA GTCCAATGTC AGATTTTGGA ACTCAACCCT
ATGAACAATG GGCCATTCAA ATGGAAAAAA AAGCTGCAAA AGAAGGAAAT
CGCAAAGAAC GTGTTTGTGC AGAACATTTG AGGAAGTACA ATGAGGCCCT
ACAAATTAAT GACACAATTC GAATGATAGA TGCGTATACT CATCTTGAAA
CTTTCTATAA TGAAGAGAAA GATAAGAAGT TTGCAGTCAT AGAAGATGAT
AGTGATGAGG GTGGTGATGA TGAGTATTGT GATGGTGATG AAGATGAGGA
TGATTTAAAG AAACCTTTGA AACTGGATGA AACAGATAGA TTTCTCATGA
CTTTATTTTT TGAAAACAAT AAAATGTTGA AAAGGCTGGC TGAAAACCCA

GAATATGAAA ATGAAAAGCT GACCAAATTA AGAAATACCA TAATGGAGCA
ATATACTAGG ACTGAGGAAT CAGCACGAGG AATAATCTTT ACAAAAACAC
GACAGAGTGC ATATGCGCTT TCCCAGTGGA TTACTGAAAA TGAAAAATTT
GCTGAAGTAG GAGTCAAAGC CCACCATCTG ATTGGAGCTG GACACAGCAG
TGAGTTCAAA CCCATGACAC AGAATGAACA AAAAGAAGTC ATTAGTAAAT
TTCGCACTGG AAAAATAAAT CTGCTTATCG CTACCACAGT GGCAGAAGAA
GGTCTGGATA TTAAAGAATG TAACATTGTT ATCCGTTATG GTCTCGTCAC
CAATGAAATA GCCATGGTCC AGGCCCGTGG TCGAGCCAGA GCTGATGAGA
GCACCTACGT CCTGGTTGCT CACAGTGGTT CAGGAGTTAT CGAACGTGAG
ACAGTTAATG ATTTCCGAGA GAAGATGATG TATAAAGCTA TACATTGTGT
TCAAAATATG AAACCAGAGG AGTATGCTCA TAAGATTTTG GAATTACAGA
TGCAAAGTAT AATGGAAAAG AAAATGAAAA CCAAGAGAAA TATTGCCAAG
CATTACAAGA ATAACCCATC ACTAATAACT TTCCTTTGCA AAAACTGCAG
TGTGCTAGCC TGTTCTGGGG AAGATATCCA TGTAATTGAG AAAATGCATC
ACGTCAATAT GACCCCAGAA TTCAAGGAAC TTTACATTGT AAGAGAAAAC
AAAGCACTGC AAAAGAAGTG TGCCGACTAT CAAATAAATG GTGAAATCAT
CTGCAAATGT GGCCAGGCTT GGGGAACAAT GATGGTGCAC AAAGGCTTAG
ATTTGCCTTG TCTCAAAATA AGGAATTTTG TAGTGGTTTT CAAAAATAAT
TCAACAAAGA AACAATACAA AAAGTGGGTA GAATTACCTA TCACATTTCC
CAATCTTGAC TATTCAGAAT GCTGTTTATT TAGTGATGAG GATTAGCACT
TGATTGAAGA TTCTTTTAAA ATACTATCAG TTAAACATTT AATATGATTA
TGATTAATGT ATTCATTATG CTACAGAACT GACATAAGAA TCAATAAAAT
GATTGTTTTA CTCTG**CATTG** **AACTCTTTTT** **AAGAACACAA** **TATATTATGC**
ATTATCCATC **TTATTGTTGG** **GCAGAGGTAA** **GGAAAATCTA** **CCAATAATTC**
TCATTAGTGT **GGAGCATTAT** **AGTCCTGTGG** **AAAGAATGCT** **GAAGTACAAA**
TGAGAATCCA **AAGTACCAGT** **CTCAGTTCTG** **TCACTAATTT** **TCAGAATAAA**
ATTAGGCAAA **TCAGTTCAAA** AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA
AAAAAAAAAA AAAAAAAAAA AAAAAAA

FIGURE 10

MSNGYSTDEN FRYLISCFRA RVKMYIQVEP VLDYLTFLPA EVKEQIQRTV
ATSGNMQAVE LLLSTLEKGV WHLGWTREFV EALRRTGSPL AARYMNPELT
DLPSPSFENA HDEYLQLLNL LQPTLVDKLL VRDVLDKCME EELLTIEDRN
RIAAAENNGN ESGVRELLKR IVQKENWFSA FLNVLRQTGN NELVQELTGS
DCSESNAEIE NLSQVDGPQV EEQLLSTTVQ PNLEKEVWGM ENNSSESSFA
DSSVVSESDT SLAEGSVSCL DESLGHNSNM GSDSGTMGSD SDEENVAARA
SPEPELQLRP YQMEVAQPAL EGKNIIICLP TGSGKTRVAV YIAKDHLDKK
KKASEPGKVI VLVNKVLLVE QLFRKEFQPF LKKWYRVIGL SGDTQLKISF
PEVVKSCDII ISTAQILENS LLNLENGEDA GVQLSDFSLI IIDECHHTNK
EAVYNNIMRH YLMQKLKNNR LKKENKPVIP LPQILGLTAS PGVGGATKQA
KAEEHILKLC ANLDAFTIKT VKENLDQLKN QIQEPCKKFA IADATREDPF
KEKLLEIMTR IQTYCQMSPM SDFGTQPYEQ WAIQMEKKAA KEGNRKERVC
AEHLRKYNEA LQINDTIRMI DAYTHLETFY NEEKDKKFAV IEDDSDEGGD
DEYCDGDEDE DDLKKPLKLD ETDRFLMTLF FENNKMLKRL AENPEYENEK
LTKLRNTIME QYTRTEESAR GIIFTKTRQS AYALSQWITE NEKFAEVGVK
AHHLIGAGHS SEFKPMTQNE QKEVISKFRT GKINLLIATT VAEEGLDIKE
CNIVIRYGLV TNEIAMVQAR GRARADESTY VLVAHSGSGV IERETVNDFR
EKMMYKAIHC VQNMKPEEYA HKILELQMQS IMEKKMKTKR NIAKHYKNNP
SLITFLCKNC SVLACSGEDI HVIEKMHHVN MTPEFKELYI VRENKALQKK
CADYQINGEI ICKCGQAWGT MMVHKGLDLP CLKIRNFVVV FKNNSTKKQY
KKWVELPITF PNLDYSECCL FSDED•

FIGURE 11

GCGCGCCGGC CTGAGAGCCC TGTGGACAAC CTCGTCATTG TCAGGCACAG
AGCGGTAGAC CCTGCTTCTC TAAGTGGGCA GCGGACAGCG GCACGCACAT
TTCACCTGTC CCGCAGACAA CAGCACCATC TGCTTGGGAG AACCCTCTCC
CTTCTCTGAG AAAGAAAGAT GTCGAATGGG TATTCCACAG ACGAGAATTT
CCGCTATCTC ATCTCGTGCT TCAGGGCCAG GGTGAAAATG TACATCCAGG
TGGAGCCTGT GCTGGACTAC CTGACCTTTC TGCCTGCAGA GGTGAAGGAG
CAGATTCAGA GGACAGTCGC CACCTCCGGG AACATGCAGG CAGTTGAACT
GCTGCTGAGC ACCTTGGAGA AGGGAGTCTG GCACCTTGGT TGGACTCGGG
AATTCGTGGA GGCCCTCCGG AGAACCGGCA GCCCTCTGGC CGCCCGCTAC
ATGAACCCTG AGCTCACGGA CTTGCCCTCT CCATCGTTTG AGAACGCTCA
TGATGAATAT CTCCAACTGC TGAACCTCCT TCAGCCCACT CTGGTGGACA
AGCTTCTAGT TAGAGACGTC TTGGATAAGT GCATGGAGGA GGAACTGTTG
ACAATTGAAG ACAGAAACCG GATTGCTGCT GCAGAAAACA ATGGAAATGA
ATCAGGTGTA AGAGAGCTAC TAAAAAGGAT TGTGCAGAAA GAAAACTGGT
TCTCTGCATT TCTGAATGTT CTTCGTCAAA CAGGAAACAA TGAACTTGTC
CAAGAGTTAA CAGGCTCTGA TTGCTCAGAA AGCAATGCAG AGATTGAGAA
TTTATCACAA GTTGATGGTC CTCAAGTGGA AGAGCAACTT CTTTCAACCA
CAGTTCAGCC AAATCTGGAG AAGGAGGTCT GGGGCATGGA GAATAACTCA
TCAGAATCAT CTTTTGCAGA TTCTTCTGTA GTTTCAGAAT CAGACACAAG
TTTGGCAGAA GGAAGTGTCA GCTGCTTAGA TGAAAGTCTT GGACATAACA
GCAACATGGG CAGTGATTCA GGCACCATGG GAAGTGATTC AGATGAAGAG
AATGTGGCAG CAAGAGCATC CCCGGAGCCA GAACTCCAGC TCAGGCCTTA
CCAAATGGAA GTTGCCCAGC CAGCCTTGGA AGGGAAGAAT ATCATCATCT
GCCTCCCTAC AGGGAGTGGA AAAACCAGAG TGGCTGTTTA CATTGCCAAG
GATCACTTAG ACAAGAAGAA AAAAGCATCT GAGCCTGGAA AAGTTATAGT
TCTTGTCAAT AAGGTACTGC TAGTTGAACA GCTCTTCCGC AAGGAGTTCC
AACCATTTTT GAAGAAATGG TATCGTGTTA TTGGATTAAG TGGTGATACC
CAACTGAAAA TATCATTTCC AGAAGTTGTC AAGTCCTGTG ATATTATTAT
CAGTACAGCT CAAATCCTTG AAAACTCCCT CTTAAACTTG GAAAATGGAG
AAGATGCTGG TGTTCAATTG TCAGACTTTT CCCTCATTAT CATTGATGAA
TGTCATCACA CCAACAAAGA AGCAGTGTAT AATAACATCA TGAGGCATTA
TTTGATGCAG AAGTTGAAAA ACAATAGACT CAAGAAAGAA AACAAACCAG
TGATTCCCCT TCCTCAGATA CTGGGACTAA CAGCTTCACC TGGTGTTGGA
GGGGCCACGA AGCAAGCCAA AGCTGAAGAA CACATTTTAA AACTATGTGC

CAATCTTGAT GCATTTACTA TTAAAACTGT TAAAGAAAAC CTTGATCAAC
TGAAAAACCA AATACAGGAG CCATGCAAGA AGTTTGCCAT TGCAGATGCA
ACCAGAGAAG ATCCATTTAA AGAGAAACTT CTAGAAATAA TGACAAGGAT
TCAAACTTAT TGTCAAATGA GTCCAATGTC AGATTTTGGA ACTCAACCCT
ATGAACAATG GGCCATTCAA ATGGAAAAAA AAGCTGCAAA AGAAGGAAAT
CGCAAAGAAC GTGTTTGTGC AGAACATTTG AGGAAGTACA ATGAGGCCCT
ACAAATTAAT GACACAATTC GAATGATAGA TGCGTATACT CATCTTGAAA
CTTTCTATAA TGAAGAGAAA GATAAGAAGT TTGCAGTCAT AGAAGATGAT
AGTGATGAGG GTGGTGATGA TGAGTATTGT GATGGTGATG AAGATGAGGA
TGATTTAAAG AAACCTTTGA AACTGGATGA AACAGATAGA TTTCTCATGA
CTTTATTTTT TGAAAACAAT AAAATGTTGA AAAGGCTGGC TGAAAACCCA
GAATATGAAA ATGAAAAGCT GACCAAATTA AGAAATACCA TAATGGAGCA
ATATACTAGG ACTGAGGAAT CAGCACGAGG AATAATCTTT ACAAAAACAC
GACAGAGTGC ATATGCGCTT TCCCAGTGGA TTACTGAAAA TGAAAAATTT
GCTGAAGTAG GAGTCAAAGC CCACCATCTG ATTGGAGCTG GACACAGCAG
TGAGTTCAAA CCCATGACAC AGAATGAACA AAAAGAAGTC ATTAGTAAAT
TTCGCACTGG AAAAATAAAT CTGCTTATCG CTACCACAGT GGCAGAAGAA
GGTCTGGATA TTAAAGAATG TAACATTGTT ATCCGTTATG GTCTCGTCAC
CAATGAAATA GCCATGGTCC AGGCCCGTGG TCGAGCCAGA GCTGATGAGA
GCACCTACGT CCTGGTTGCT CACAGTGGTT CAGGAGTTAT CGAACATGAG
ACAGTTAATG ATTTCCGAGA GAAGATGATG TATAAAGCTA TACATTGTGT
TCAAAATATG AAACCAGAGG AGTATGCTCA TAAGATTTTG GAATTACAGA
TGCAAAGTAT AATGGAAAAG AAAATGAAAA CCAAGAGAAA TATTGCCAAG
CATTACAAGA ATAACCCATC ACTAATAACT TTCCTTTGCA AAAACTGCAG
TGTGCTAGCC TGTTCTGGGG AAGATATCCA TGTAATTGAG AAAATGCATC
ACGTCAATAT GACCCCAGAA TTCAAGGAAC TTTACATTGT AAGAGAAAAC
AAAGCACTGC AAAAGAAGTG TGCCGACTAT CAAATAAATG GTGAAATCAT
CTGCAAATGT GGCCAGGCTT GGGGAACAAT GATGGTGCAC AAAGGCTTAG
ATTTGCCTTG TCTCAAAATA AGGAATTTTG TAGTGGTTTT CAAAAATAAT
TCAACAAAGA AACAATACAA AAAGTGGGTA GAATTACCTA TCACATTTCC
CAATCTTGAC TATTCAGAAT GCTGTTTATT TAGTGATGAG GATTAGCACT
TGATTGAAGA TTCTTTTAAA ATACTATCAG TTAAACATTT AATATGATTA
TGATTAATGT ATTCATTATG CTACAGAACT GACATAAGAA TCAATAAAAT
GATTGTTTTA CTCTG

FIGURE 12

MSNGYSTDEN FRYLISCFRA RVKMYIQVEP VLDYLTFLPA EVKEQIQRTV
ATSGNMQAVE LLLSTLEKGV WHLGWTREFV EALRRTGSPL AARYMNPELT
DLPSPSFENA HDEYLQLLNL LQPTLVDKLL VRDVLDKCME EELLTIEDRN
RIAAAENNGN ESGVRELLKR IVQKENWFSA FLNVLRQTGN NELVQELTGS
DCSESNAEIE NLSQVDGPQV EEQLLSTTVQ PNLEKEVWGM ENNSSESSFA
DSSVVSESDT SLAEGSVSCL DESLGHNSNM GSDSGTMGSD SDEENVAARA
SPEPELQLRP YQMEVAQPAL EGKNIIICLP TGSGKTRVAV YIAKDHLDKK
KKASEPGKVI VLVNKVLLVE QLFRKEFQPF LKKWYRVIGL SGDTQLKISF
PEVVKSCDII ISTAQILENS LLNLENGEDA GVQLSDFSLI IIDECHHTNK
EAVYNNIMRH YLMQKLKNNR LKKENKPVIP LPQILGLTAS PGVGGATKQA
KAEEHILKLC ANLDAFTIKT VKENLDQLKN QIQEPCKKFA IADATREDPF
KEKLLEIMTR IQTYCQMSPM SDFGTQPYEQ WAIQMEKKAA KEGNRKERVC
AEHLRKYNEA LQINDTIRMI DAYTHLETFY NEEKDKKFAV IEDDSDEGGD
DEYCDGDEDE DDLKKPLKLD ETDRFLMTLF FENNKMLKRL AENPEYENEK
LTKLRNTIME QYTRTEESAR GIIFTKTRQS AYALSQWITE NEKFAEVGVK
AHHLIGAGHS SEFKPMTQNE QKEVISKFRT GKINLLIATT VAEEGLDIKE
CNIVIRYGLV TNEIAMVQAR GRARADESTY VLVAHSGSGV IEHETVNDFR
EKMMYKAIHC VQNMKPEEYA HKILELQMQS IMEKKMKTKR NIAKHYKNNP
SLITFLCKNC SVLACSGEDI HVIEKMHHVN MTPEFKELYI VRENKALQKK
CADYQINGEI ICKCGQAWGT MMVHKGLDLP CLKIRNFVVV FKNNSTKKQY
KKWVELPITF PNLDYSECCL FSDED•